OVERVIEW OF THE NEW CDC SELECT AGENT RULE: *42 C.F.R. Part 73*

2004 Public Health Series on Infectious Diseases
National Laboratory Training Network
October 20, 2004

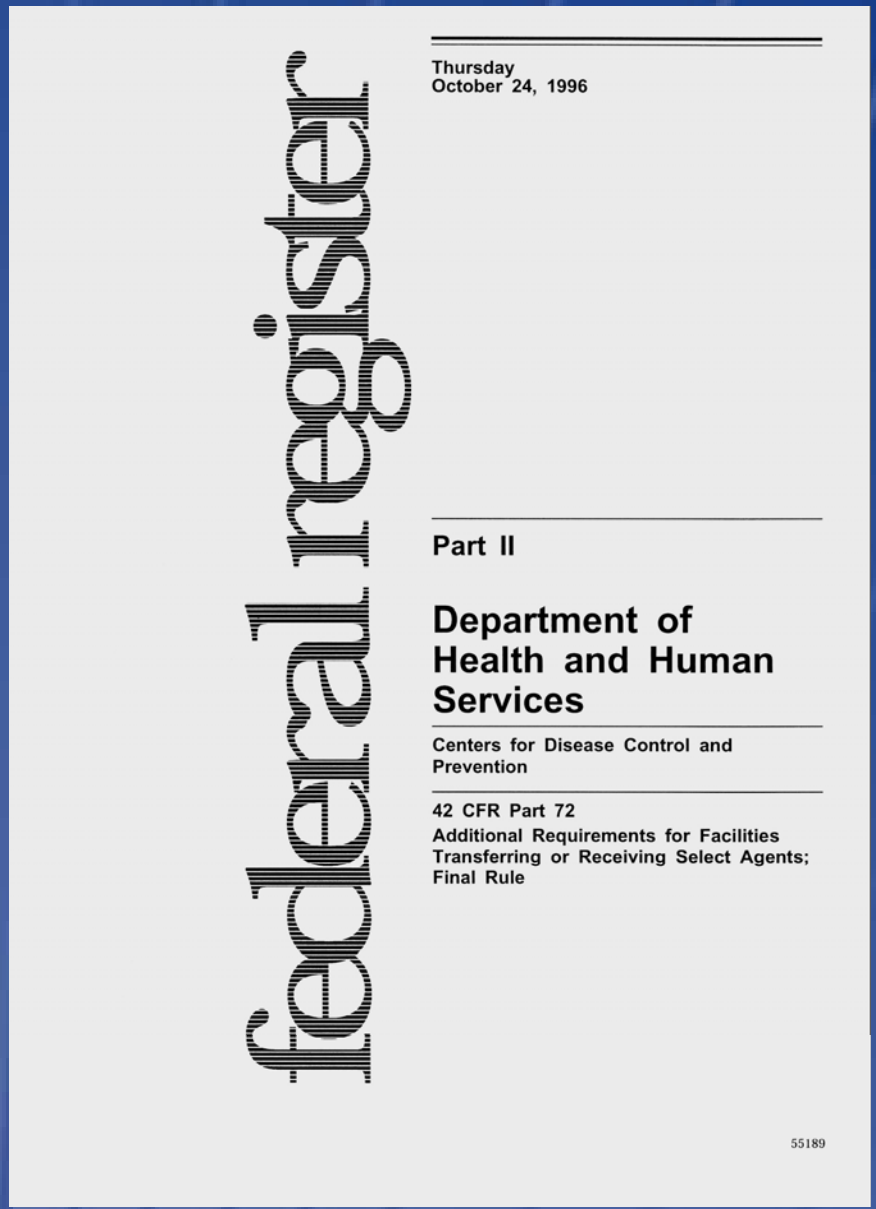
Select Agent Program
Office of Terrorism Preparedness
and Emergency Response
Centers for Disease Control and Prevention

Antiterrorism and Effective Death Penalty Act of 1996

Sec. 511. Enhanced Penalties and Control of Biologic Agents
Public Law 104-132; April 24, 1996

The Secretary of HHS shall, through regulation:

- Maintain a list of biological agents that have the potential to pose a severe threat to public health and safety.
- Establish procedures for the transfer of the listed biological agents, including measures to ensure:
  - Proper training and appropriate skills to handle agents.
  - Proper laboratory facilities to contain and dispose of agents.


federal register

Thursday
October 24, 1996

Part II

Department of Health and Human Services

Centers for Disease Control and Prevention

42 CFR Part 72

Additional Requirements for Facilities Transferring or Receiving Select Agents; Final Rule

55189

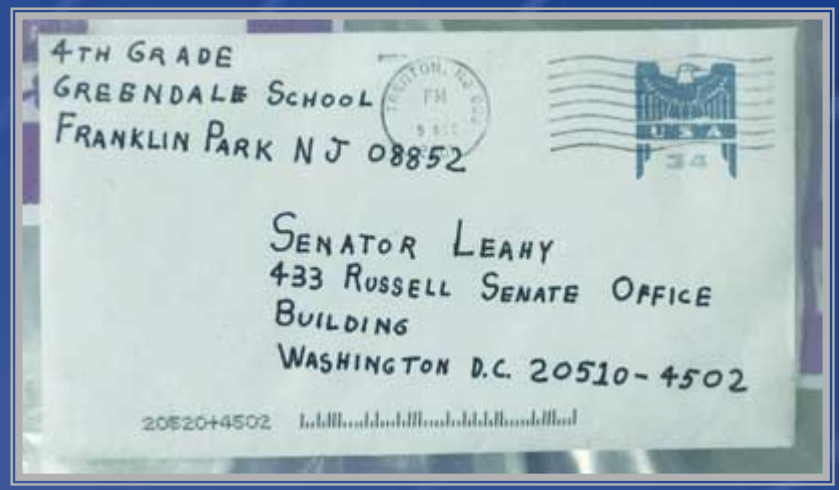
Title 42 Part 72.6 “The Select Agent Rule”

Effective date: April 15, 1997

Fundamental Components of the Regulation (42 C.F.R. 72.6)

1. A list of biological agents (select agents)
2. Registration of facilities transferring these agents
   - Designate Responsible Facility Official
   - Meet requirements to safely handle the agent
3. Transfer requirements
   - EA-101
4. Verification procedures
   - Inspection
5. Agent disposal requirements
6. Research and clinical exemptions

Post - September 11, 2001



USA PATRIOT Act
(Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001)

Public Law 107-56 Signed: 10/23/2001

- Sec. 175b. Possession by Restricted Persons
  - No restricted person shall ship, possess, or receive a Select Agent.

Public Health Security and Bioterrorism Preparedness and Response Act of 2002

Signed: June 12, 2002

- Significantly changed the regulatory authorities of HHS under Sec. 511 of the "Antiterrorism and Effective Death Penalty Act of 1996."
- Granted comparable regulatory authorities to USDA for biological agents and toxins that present a severe threat to plant or animal health, or animal or plant products.
- Select agents and toxins subject to regulation by both agencies (''overlap''). Required coordination between USDA and HHS on "overlap" agents regulated by both agencies.

Coordination with USDA / APHIS

- If an entity has overlap agents, the entity may register with either CDC or APHIS
- Agencies will coordinate approvals of entities with overlap agents
  - ➢Requires concurrence of other agency
- Registration package and other forms are the same for both agencies

Public Health Security and Bioterrorism Preparedness and Response Act of 2002

Signed: June 12, 2002

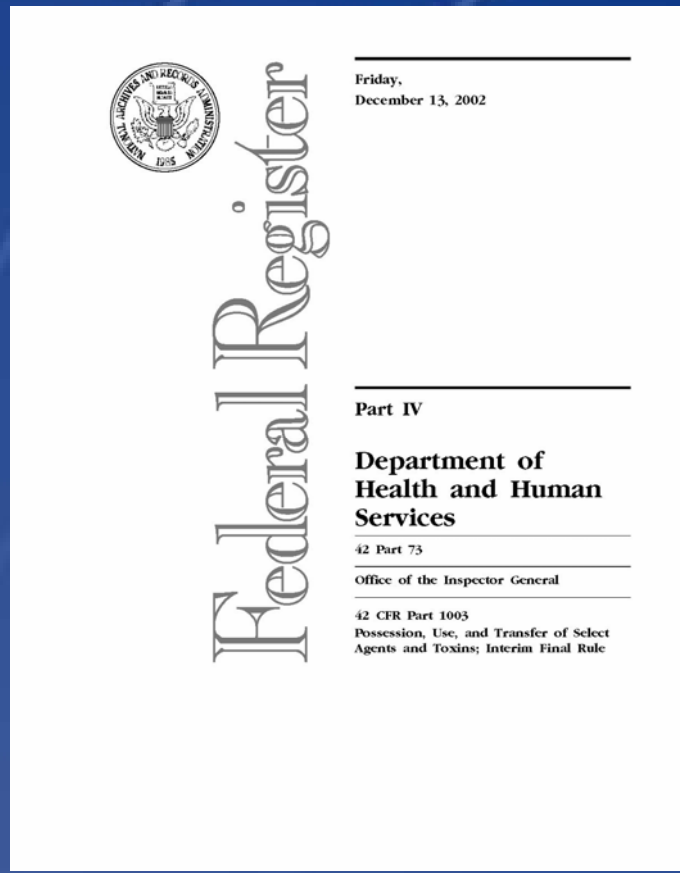
Summary:

- Registration for possession, use, and transfer
- Establish requirements for safety and security
- Electronic Database check by DOJ (Security Risk Assessment = "SRA")
  - Entity and individual
  - Restricted persons (USA PATRIOT Act)
- Specifies exemptions
- Federal nondisclosure protection of sensitive site-specific information
- Additional criminal penalties
- Notification of theft, loss, or release
- National database
- Immediate one time notification

Possession, Use, and Transfer of Select Agents and Toxins

42 C.F.R. Part 73, 9 C.F.R. Part 121, and 7 C.F.R. Part 331

- Effective date: February 7, 2003
- Phase-in of new requirements:
  - March 12, 2003 – New transfer provisions
  - April 12, 2003 – Security Risk Assessments for individuals submitted
  - June 12, 2003 – Developed security plan
  - Sept. 12, 2003 – Implemented security plan
  - Nov. 12, 2003 – Full compliance for registration



CDC™

OVERVIEW OF REGULATION
42 C.F.R. Part 73

- List of Select Agents and Toxins (HHS and Overlap)
  - Updates list of select agents and toxins
  - **http://www.cdc.gov/od/sap/docs/salist.pdf**

Establishment of Select Agent Lists

- Technical Advisory Committee
  - **Effect on human and animal health**
  - **Degree of contagiousness**
  - Mode of transmission
  - Available vaccine and therapy
  - Other criteria as appropriate
- Federal Register publication and comment

Changes To Select Agent List

Federal Register August 23, 2002

Deletions	Additions
Hantavirus	Herpes B
Yellow fever	Monkeypox
Aflatoxins	*C. posadasii*

Clarifications: Variola; botulinum; shigatoxin

Types of Select Agents and Toxins

- HHS-only Agents (HHS has sole authority and responsibility to regulate)
  - Select agents and toxins that may affect public health and safety
- USDA-only Agents (USDA has sole authority and responsibility to regulate)
  - Select agents and toxins that may affect animal and plant health and animal and plant products
- "Overlap Agents"
  - Select agents and toxins subject to regulation by both agencies

- The Act provides for interagency coordination between the two departments regarding overlap select agents and toxins

HHS, USDA, & Overlap Select Agents And Toxins

	HHS	Overlap	USDA
Viruses	9	4	21
Bacteria	3	9	2
Fungi	1	1	0
Toxins	7	5	0
Plant Path	0	0	10
	20	19	33

OVERVIEW OF REGULATION
42 C.F.R. Part 73

- List of Select Agents and Toxins (HHS and Overlap)
  - Updates list of select agents and toxins
  - Regulates toxins based on potency and quantity

Toxin Specifications

- Established cutoff amounts for the possession of each toxin based on its potency.
- Established amounts based on how much one could safely possess without constituting a potential threat to public safety or raising concerns about use as a weapon that would have a widespread effect.
- Ruled out small amounts of toxins for assassination purposes.
- Not required to register if the aggregate amount of a toxin under the control of a principal investigator is below the amount specified.

HHS And Overlap Toxins

- Botulinum neurotoxins (0.5 mg)
- Staphylococcal enterotoxins (5 mg)
- Abrin (100 mg)
- *Clostridium perfringens* epsilon toxin (100 mg)
- Conotoxins (100 mg)
- Ricin (100 mg)
- Saxitoxin (100 mg)
- Shigatoxin (100 mg)
- Shiga-like ribosome inactivating proteins (100 mg)
- Tetrodotoxin (100 mg)
- Diacetoxyscirpenol (1,000 mg)
- T-2 toxin (1,000 mg)

If the aggregate amount under the control of a principal investigator exceeds the amount specified

OVERVIEW OF REGULATION
42 C.F.R. Part 73

- List of Select Agents and Toxins (HHS and Overlap)
  - Updates list of select agents and toxins
  - Regulates toxins based on potency and quantity
  - Updates Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms

Genetic Elements, Recombinant Nucleic Acids, And Recombinant Organisms

- Nucleic acids (synthetic or naturally derived, contiguous or fragmented, in host chromosomes or in expression vectors) that can encode infectious and/or replication competent forms of any of the select agent viruses.
- Nucleic acids (synthetic or naturally derived) that encode for the functional form(s) of any of the toxins listed if the nucleic acids:
  - Are in a vector or host chromosome and/or can be expressed in vivo or in vitro.
- Listed viruses, bacteria, fungi, and toxins that have been genetically modified.

Restricted Experiments
§ 73.10(c) Safety

(c) An entity may not conduct the following experiments unless approved by the HHS Secretary after consultation with experts:

- (1) Experiments utilizing recombinant DNA that involve the deliberate transfer of a drug resistance trait to select agents that are not known to acquire the naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture. *[NIH Guidelines: Major Action, RAC approval]*
- (2) Experiments involving the deliberate formation of recombinant DNA containing genes for the biosynthesis of select toxins lethal vertebrates at an LD_{50} < 100 ng/kg weight. *[NIH Guidelines: Require NIH/OBA and IBC approval]*

OVERVIEW OF REGULATION
42 C.F.R. Part 73

- List of Select Agents and Toxins (HHS and Overlap)
  - Updates list of select agents and toxins
  - Regulates toxins based on potency and quantity
  - Updates Genetic Elements, Recombinant Nucleic Acids, and Recombinant Organisms
  - Allows for exclusions & exemptions

§ 73.4 & 73.5 Exclusions

- Select agents or toxins in their naturally occurring environment, provided that it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source.
- Non-viable select agent organisms or nonfunctional toxins.
- Entities with specific quantities of toxins under the control of a principal investigator.

Requesting an Exclusion of an Attenuated Strain

- CDC may exclude attenuated strains of select agents or toxins upon a determination that they do not pose a severe threat to the public health and safety
- To apply: submit a request in writing to the CDC Select Agent Program
  - Must provide documentation establishing that the attenuated strain is eligible for exclusion
- An exclusion is effective upon notification to the applicant and are listed on the CDC Web site at http://www.cdc.gov/od/sap

42 C.F.R. Part 73.6 Exemptions

- Clinical or Diagnostic Laboratories
  - Agents used only for diagnosis, verification, or proficiency testing (no reference or retention allowed)
  - Transferred or destroyed after identification
  - Notify federal and state authorities
  - Complete CDC Form 0.1318
- Products approved under a Federal Act
- Investigational products
  - Must apply for exemption, CDC Form 0.1317
- Public health or agricultural emergency
  - Must apply for exemption, CDC Form 0.1317

Under The New Select Agent Regulation An Entity Must

- Register for each select agent or toxin it possesses, uses, or transfers
- Designate a Responsible Official (RO)
- Receive government approval of entity (owners), RO, & individuals who need access to select agents
  - Based on DOJ check of electronic databases ("Security Risk Assessment" = SRA)
- Receive prior approval of all transfers
- Provide notification of theft, loss, or release of a select agent or toxin

An Entity Must Also

- Maintain records:
  - Inventories
  - Access to agents
  - Access to areas where agents are stored or used
  - Transfer documents
- Develop an emergency response plan
- Develop and implement safety and security plans
- Conduct safety and security training

42 CFR 73.10 Safety

Develop and implement a safety plan:

- For BSL 2-4 select agents:
  - Biosafety in Microbiological and Biomedical Laboratories, Fourth edition, May 1999.
- For toxin select agents:
  - 29 CFR 1910.1450 Occupational Exposure to Hazardous Chemicals in Laboratories.
  - 29 CFR 1910.1200 Hazard Communication.
  - Appendix I: Guidelines for Work with Toxins of Biological Origin.
- For recombinant select agents:
  - Guidelines for research involving recombinant DNA molecules (NIH Guidelines), April 2002.

42 CFR 73.11 Security
Security Plan

- An entity must develop and implement a security plan establishing policy and procedures that ensure the security of areas containing select agents and toxins.

- Additional guidance
  - "Laboratory Security and Emergency Response Guidance for Laboratories Working with Select Agents". *MMWR* December 6, 2002. Updates Appendix F of the current *BMBL.*

42 C.F.R. 73.11 Security

- Allow access to select agents & toxins only to individuals who have an approved SRA

- Access means:
  - *The ability to gain possession of a select agent or toxin*

42 C.F.R. 73.11 Security

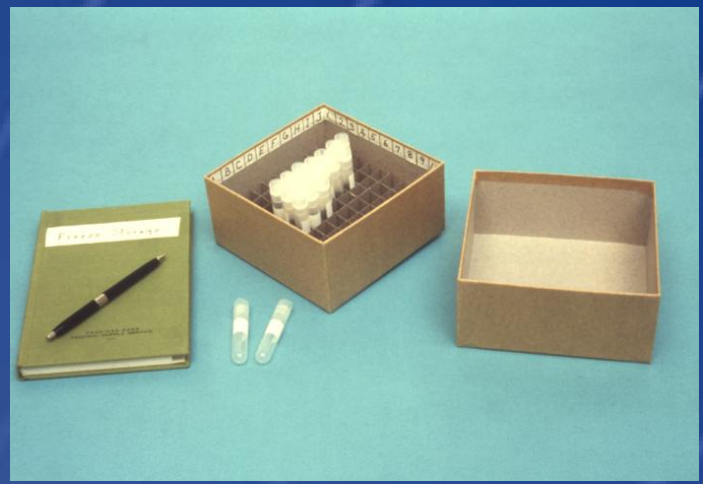
- Individuals without an approved SRA may be denied access to select agents & toxins by the use of physical or personnel barriers:
  - Physical barriers
    - Locks on doors and storage containers
    - Card or key pads
  - Personnel barriers
    - Must be escorted and continually monitored by an individual with an approved SRA
    - Allows for access to the area but not to the select agent or toxin (e.g., maintenance, repair, cleaning)

42 CFR 73.15 Records

- Access records
  - Current list of individuals with an approved SRA for access to select agents or toxins
  - For access to an area where select agents or toxins are used or stored:
    - Name, date, & time entered / left
    - When denying access by escort of individuals not approved for access to select agents or toxins (e.g., maintenance, repair, cleaning) must identify the approved escort
  - For access to select agents or toxins:
    - Name, agent used, date

42 CFR 73.15 Records

- Inventory
  - Agent name, characteristics, & source
  - Account for agents (viable) in long-term storage
  - Account for amount of toxin at all times
- Transfer documents
  - Sender / receiver, date and amount acquired or transferred
    - EA-101 Forms
    - Intra-entity transfer documents



SECURITY RISK ASSESSMENT

- All individuals needing access to select agents or toxins and owners of entities seeking to register must have a security risk assessment (database and fingerprint check) conducted by the Attorney General.
- The Attorney General has designated the Federal Bureau of Investigation (FBI), Criminal Justice Information Services Division (CJIS), to conduct the security risk assessments.
- CJIS sends results to lead agency (CDC or APHIS)
- Lead agency is responsible for reporting results back to the entity

FBI – SECURITY RISK ASSESSMENT
Prohibited Categories

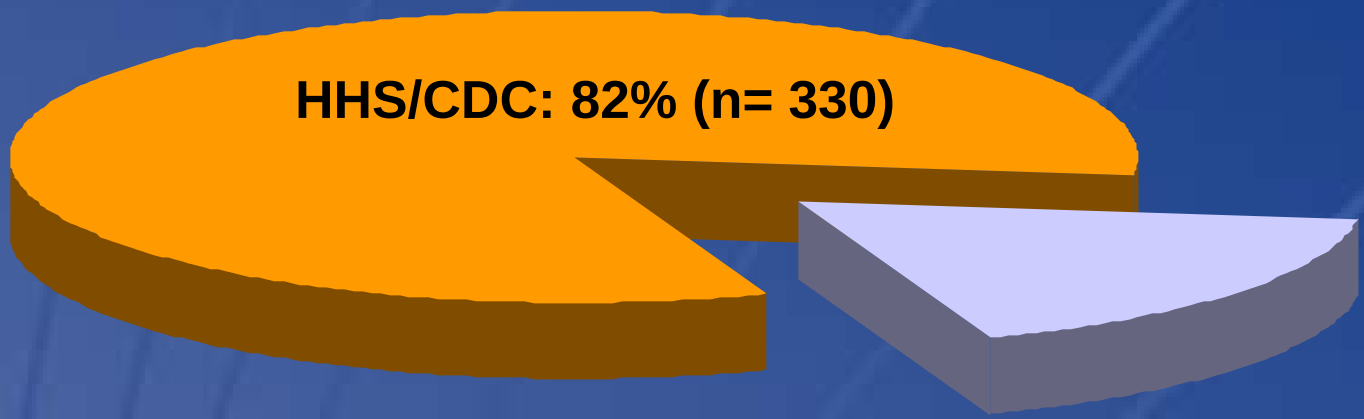
- A restricted person under 18 U.S.C. 175b (USA PATRIOT Act)
- Reasonably suspected by any Federal law enforcement or intelligence agency of:
  - Committing a crime specified in 18 U.S.C. 2332b(g)(5);
  - Having a knowing involvement with an organization that engages in domestic or international terrorism (as defined in 18 U.S.C. 2331) or with any other organization that engages in intentional crimes of violence; or
  - Being an agent of a foreign power (as defined in 50 USC 1801).

Penalties

- Civil Money
  - Up to $250,000 for an individual for each violation
  - Up to $500,000 for an organization for each violation
- Criminal
  - Imprisonment for up to 5 years, a fine, or both for:
    - Transfer of a select agent to an unregistered person
    - Possession of a select agent by an unregistered person
    - Knowingly making a false statement

Number of Entities Registering a Select Agent or Toxin with HHS/CDC or USDA/APHIS

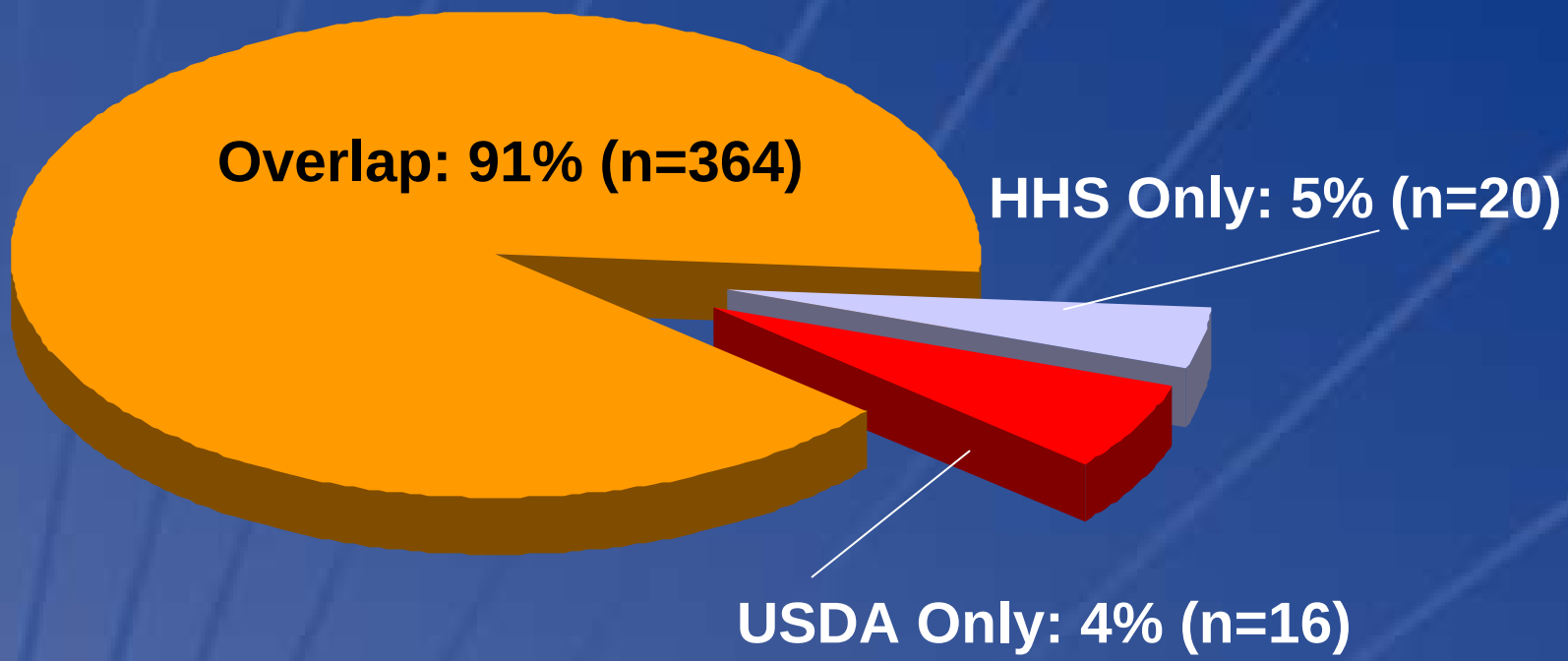
(n = 400 applications)



USDA/APHIS: 18% (n=70)

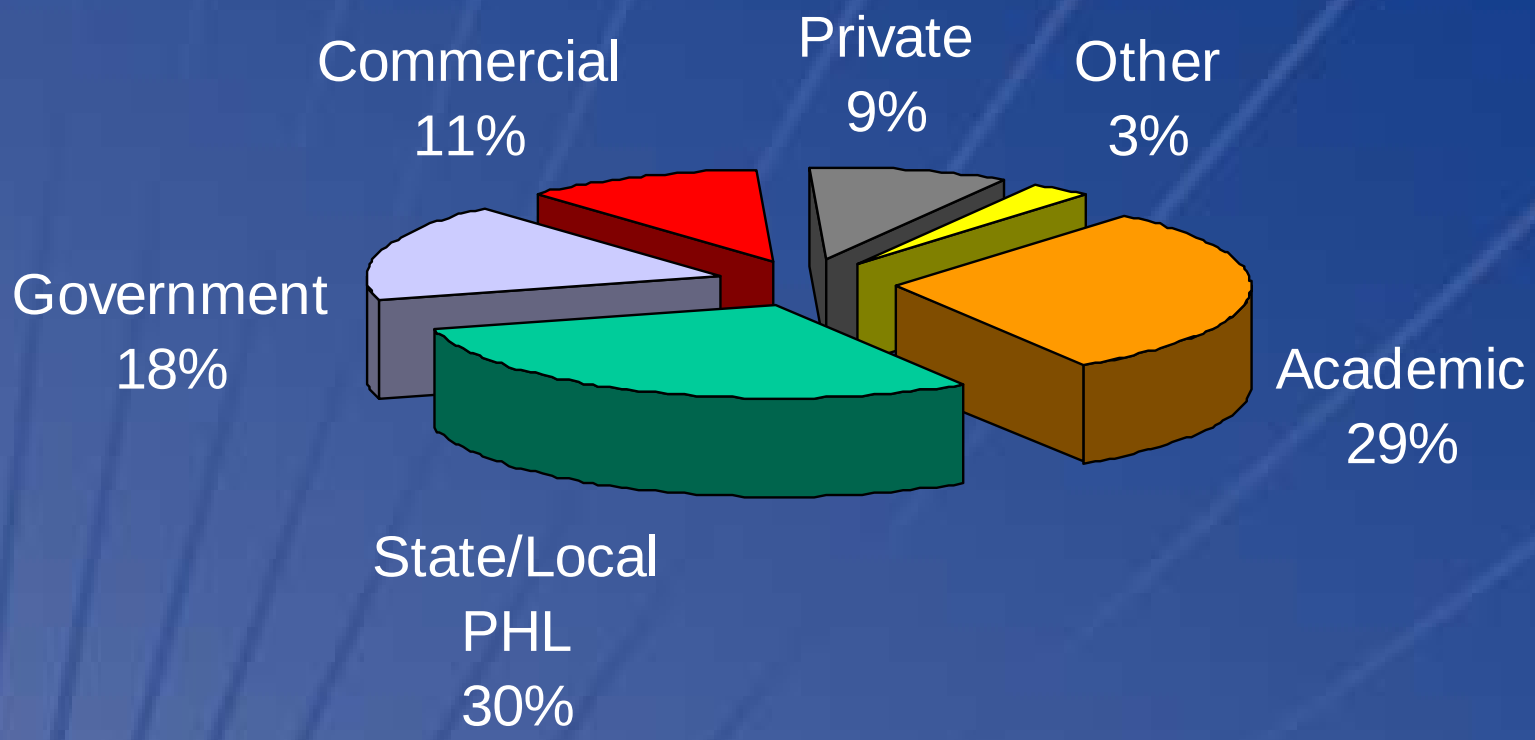
Type of Select Agent or Toxin Registered under 42 C.F.R. 73, 9 C.F.R. 121 or 7 C.F.R. 331

(n=400)



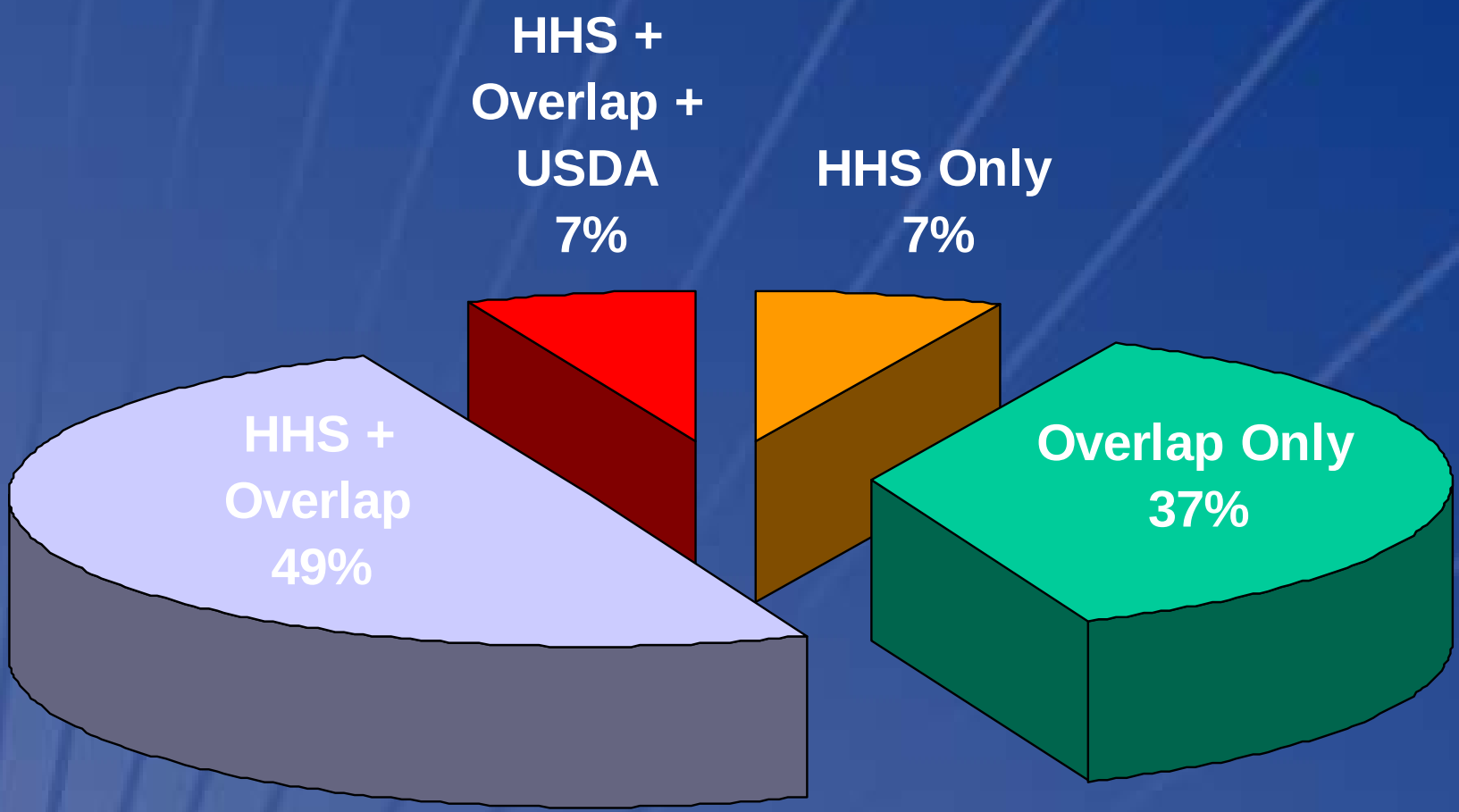
Types of CDC-Lead Entities Registered

(N = 330 Active)



Types of CDC-Lead Entities Registered

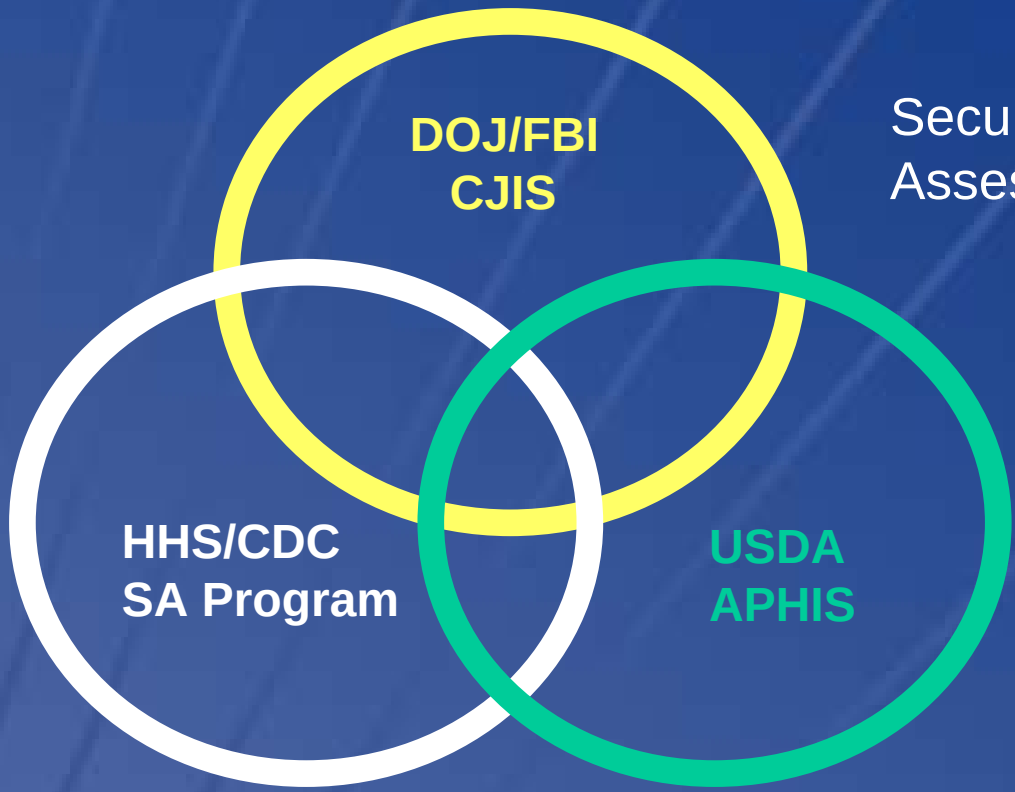
(N = 330)



Coordination with USDA/APHIS

- CDC and APHIS working diligently to harmonize efforts and reduce burden on entity:
  - single registration system
  - Entities should interface with only one agency
  - CDC/APHIS plan to provide increased communication and outreach to the regulated community
- Inspections
  - APHIS has additional regulatory requirements for importation or interstate transfer of overlap and USDA-only agents (7 C.F.R. Part 330 and 9 C.F.R. Part 122)
    - Requires approval of permit application
    - May require inspection
    - For CDC-lead entities, APHIS is currently accepting CDC inspections to minimize burden on entities

Federal Partners



Security Risk Assessments

42 CFR 73

7 CFR 331
9 CFR 121

Next in 2004 - 2005

- Final Rule
  - Review comments received on Interim Final Rule (n=111)
  - Publication anticipated Fall 2004
- 2004-2005 secure web-based registration system
- Training initiatives (e.g., workshops, videos)
  - October 17, 2004. Workshop. 47th Annual Meeting of ABSA in San Antonio. Select Agents Regulations: Overview and General Requirements.
  - June, 2005. Select Agent Workshop. 105th General Meeting of ASM in Atlanta.

For More Information

- CDC Select Agent Program
  - Phone 404-498-2255
  - Fax 404-498-2265
  - E-mail lrsat@cdc.gov
  - Web site http://www.cdc.gov/od/sap
- USDA/APHIS
  - Phone 301-734-3277
  - Fax 301-734-3652
  - Web site http://www.aphis.usda.gov/vs/ncie/bta.html
- FBI
  - Phone 304-625-4900
  - Fax 304-625-5393
  - Web site http://www.fbi.gov/hq/cjisd/cjis.htm

QUESTIONS?????

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